AMENDMENTS TO THE CLAIMS

1-2. (Canceled)

3. (Previously presented) The composition of Claim 34, wherein the therapeutic,

diagnostic, or prophylactic agent is a protein, peptide, nucleotide, oligonucleotide, saccharide,

polysaccharide, organic molecule, or combination thereof.

4. (Currently amended) The composition of Claim 36, wherein the hydrophobic

component is a synthetic vinyl-type hydrophobic polymer, a non-vinyl-type-hydrophobic

polymer, naturally derived polymer, a membrane disruptive peptide, or a phospholipid bilayer

disrupting agent.

5-7. (Canceled)

8. (Previously presented) The composition of Claim 36, wherein the pH-sensitive

linkage is an acetal, orthoester, cis-aconityl group, hydrazone, ester, Schiff base, vinyl ether,

dithioacetal, tert butyl ester, carbamate, thioester, or phosphoramidate.

9. (Previously presented) The composition of Claim 34, wherein the therapeutic,

diagnostic, or prophylactic agent is coupled to either the hydrophilic or the hydrophobic

component by a degradable or disruptable linkage.

10-12. (Canceled)

13. (Previously presented) The composition of Claim 36, wherein the conjugate

further comprises a ligand, wherein the ligand specifically binds to a target molecule.

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Seattle, Washington 98101 206.682.8100 14. (Previously presented) The composition of Claim 34, wherein the therapeutic,

diagnostic, or prophylactic agent is complexed to a component of the conjugate.

15. (Previously presented) The composition of Claim 36, wherein the pH sensitive

linkage is hydrolyzed within about 30 to 60 minutes at a pH between 5.0 and 5.5.

16. (Previously presented) The composition of Claim 36 further comprising a

pharmaceutically acceptable carrier for delivery of the conjugate to a cell or organelle.

17. (Previously presented) The composition of Claim 16, wherein the carrier

provides for systemic delivery of the conjugate, local delivery of the conjugate, or topical

delivery of the conjugate.

18. (Canceled)

19. (Previously presented) The composition of Claim 34, wherein the therapeutic,

diagnostic, or prophylactic agent is an antisense nucleotide, ribozyme, ribozyme guide sequence,

triplex forming oligonucleotide, or gene.

20-33. (Canceled)

34. (Previously presented) The composition of Claim 36 further comprising an agent,

wherein the agent is a therapeutic, diagnostic, or prophylactic agent.

35. (Previously presented) The composition of Claim 36, wherein the hydrophobic

component comprises a synthetic polymer.

36. (Currently amended) A composition for enhancing transport through a

membrane, comprising a water-soluble hydrophilic conjugate having a hydrophobic component

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Seattle, Washington 98101 206.682.8100 linked to a hydrophilic component by a pH-sensitive linkage, wherein the pH-sensitive linkage is stable at a pH between 6.8 and 8 and hydrolyzed at a pH less than 6.5 to release the hydrophobic component, wherein the hydrophilic component comprises a polyalkylene oxide, wherein the hydrophobic component is a vinyl-type polymer, and wherein the hydrophobic component is membrane disruptive and allows enhanced transport through a membrane [[only]] when released from the hydrophilic conjugate.

37. (Canceled)

38. (Currently amended) A <u>water-soluble</u> conjugate, comprising:

(a) a hydrophobic synthetic vinyl-type polymer, wherein the polymer is

endosomal membrane disruptive when released from the hydrophilic conjugate;

(b) a plurality of pendant hydrophilic polyalkylene oxide components; and

(c) a plurality of pH-sensitive linkages, wherein each of the pendant

polyalkylene oxide components is covalently linked to the polymer through a pH-sensitive

linkage that is stable at a pH between 6.8 and 8 and hydrolyzed at a pH less than 6.5.

39. (Previously presented) The conjugate of Claim 38, wherein the synthetic

vinyl-type polymer is a terpolymer of dimethylaminoethyl methacrylate, butyl methacrylate, and

styrene benzaldehyde.

40. (Previously presented) The conjugate of Claim 38, wherein the pH-sensitive

linkage is selected from the group consisting of an acetal, a dithioacetal, an ester, an orthoester,

and a carbamate.

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- 41. (Currently amended) A composition, comprising:
 - (a) a water-soluble hydrophilic conjugate comprising:
- (i) a hydrophobic synthetic vinyl-type polymer, wherein the polymer is endosomal membrane disruptive when released from the hydrophilic conjugate;
- (ii) a plurality of pendant hydrophilic polyalkylene oxide components; and
- (iii) a plurality of pH-sensitive linkages, wherein each of the pendant polyalkylene oxide components is covalently linked to the polymer through a pH-sensitive linkage that is stable at a pH between 6.8 and 8 and hydrolyzed at a pH less than 6.5; and
 - (b) a therapeutic or diagnostic agent.
- 42. (Previously presented) The composition of Claim 41, wherein the synthetic vinyl-type polymer is a terpolymer of dimethylaminoethyl methacrylate, butyl methacrylate, and styrene benzaldehyde.
- 43. (Previously presented) The composition of Claim 41, wherein the pH-sensitive linkage is selected from the group consisting of an acetal, a dithioacetal, an ester, an orthoester, and a carbamate.
- 44. (Previously presented) The composition of Claim 41, wherein the therapeutic or diagnostic agent is selected from the group consisting of a protein, a peptide, a saccharide, a polysaccharide, an organic molecule, a nucleotide, an antisense nucleotide, an oligonucleotide, a ribozyme, a ribozyme guide sequence, a triplex forming oligonucleotide, and a gene.

45. (New) The composition of Claim 36, wherein the hydrophobic component

comprises a random, block, or graft copolymer, wherein the copolymer comprises an alkyl

substituted or unsubstituted acrylate group.

46. (New) The composition of Claim 36, wherein the hydrophobic component

comprises poly(ethylacrylic acid), poly(propylacrylic acid), poly(butylacrylic acid), or acrylic

acid polymer and copolymers.

47. (New) A composition for enhancing transport through a membrane, comprising a

hydrophilic conjugate having a hydrophobic component linked to a hydrophilic component by a

pH-sensitive linkage,

wherein the pH-sensitive linkage is stable at a pH between 6.8 and 8 and hydrolyzed at a

pH less than 6.5 to release the hydrophobic component;

wherein the hydrophilic component comprises a polyalkylene oxide;

wherein the hydrophobic component comprises a random, block, or graft copolymer,

wherein the copolymer comprises an alkyl substituted or unsubstituted acrylate group; and

wherein the hydrophobic component is membrane disruptive and allows enhanced transport

through a membrane when released from the hydrophilic conjugate.

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